

# Pediatric Bipolar Disorder

Diagnostic Challenges in Identifying Symptoms and Course of Illness

his article reviews the challenges associated with diagnosing pediatric bipolar disorder. The article also reviews and provides discussion on the assessment tools, complex mood cycling, and clinical symptoms of pediatric bipolar disorder. The challenge of differentiating common comorbid disorders like attention deficit hyperactivity disorder and conduct disorder from pediatric bipolar disorder is presented and discussed. A discussion of the validity of diagnosis in longitudinal studies is also provided.

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# INTRODUCTION

For the general population, a conservative estimate of an individual's risk of having full-blown bipolar disorder is one percent. Disorders in the bipolar spectrum may affect 4 to 6 percent. When one parent has bipolar disorder, the risk to each child is 15 to 30 percent. When both parents have bipolar disorder, the risk increases to 50 to 75 percent. The risk in siblings and fraternal twins is 15 to 25 percent. The risk in identical twins is approximately 70 percent.<sup>1,2</sup> More than 60 percent of adult patients with bipolar disorder report onset of their mood symptoms before the age of 20.1-4 Retrospective interviews of a large sample of adult bipolar disorder patients indicated that approximately 30 percent experienced very early onset of their symptoms (age 13 or younger) and approximately 40 percent experienced early onset (age 13-18).5

Phenomenology and clinical prevalence of pediatric bipolar disorder has always been controversial. But accumulating evidence of recent, rapid increase in the rate of diagnosis has further increased the interest in the reliability and validity of diagnosis of bipolar disorder in children and adolescents. A study published recently suggested that the number of young people diagnosed with bipolar disorder in outpatient settings has increased 40-fold in the United States (US) between 1994 and 2003. For individuals age 19 years and younger, diagnosis was made 25 of 100,000 visits (about 20,000 patients) in 1994. This number has grown to 1,003 per 100,000 visits (about 80,000 patients) in 2002 to 2003. Another study performed on an inpatient population also suggested an almost six-fold increase in pediatric bipolar diagnosis between 1996 and 2004.7

The purpose of this paper is to examine the diagnostic challenges in identifying pediatric bipolar disorder and our contemporary understanding of the clinical symptoms and course of this illness.

### **DIAGNOSTIC CHALLENGE**

One of the main issues in pediatric bipolar disorder is how to properly diagnose it. On average, it takes 10 years before bipolar patients are properly diagnosed and treated.8 For each year of untreated illness, bipolar youth have a 10percent lower likelihood of recovery.8 It is universally accepted that clinical presentation of bipolar disorder in children is significantly different than adults.9 But unfortunately in the Diagnostic and Statistical Manual of Mental Disorders (DSM) revisions published since the third edition (IV and IV, Text Revision), adult criteria have been used to diagnose bipolar disorder in children. To illustrate how difficult it is to use the DSM-IV to diagnose bipolar disorder in children, the manual says that a hypomanic episode requires a "distinct period of persistently elevated, expansive, or irritable mood lasting throughout at least four days."10 However, over 70 percent of children with the illness have been found to have mood and energy shifts several times a day.11,12 Developmentally speaking, children, who have yet to achieve emotional, neurocognitive, and physical maturity, always present a diagnostic challenge. Labile, unstable, and changeable mood is prominent, especially in children younger than 10 years. Children and adolescents find it difficult to verbalize their emotions, and symptoms can have different meanings based on the developmental level of the child. There is a high rate of comorbid psychiatric disorders in pediatric bipolar disorder (especially attention deficit hyperactivity disorder [ADHD] in prepubertal children), and significant symptom overlap in common comorbid conditions makes the task of reaching accurate diagnosis even more difficult.9,13

### **ASSESSMENT**

**Interviews.** A careful interview with comprehensive evaluation of

all clinically relevant symptoms conducted by a clinician knowledgeable about mood disorders in children and adolescents is essential. 13 It is important to interview, at minimum, the child and one parent. Discrepancies between informants are common.14,15 A study comparing separate child and parent interview data for pediatric bipolar disorder concluded that parent-child concordance was poor to fair for all cardinal and non-cardinal mania symptoms. Symptoms endorsed by just the child included substantial proportions of clinical symptoms that best differentiate mania from ADHD (i.e., elation, grandiosity, flight of ideas, racing thoughts, decreased need for sleep).16 It is helpful for families to keep daily logs for at least a two-week period before their first clinic visit. Ideally, caregivers need to track mood, energy, sleep, and unusual behavior in the child. Before ascertaining symptom presence and absence, children and parents should always be asked about functioning at home, at school, and with peers.<sup>13</sup> The FIND approach can be helpful in the assessment of seriousness of the symptoms.<sup>13</sup> The acronym FIND stands for the following:

- Frequency—symptoms occur most days in a week
- Intensity—severity of symptoms is enough to cause moderate to severe disturbance
- Number—symptoms occur 3 to 4 times a day
- Duration—symptoms occur 4 or more hours a day.

Such a guideline can be useful in developing a clinically useful threshold, which can be vital in reaching the correct diagnosis.

**Rating scales.** Some of the prominent instruments/rating scales used in pediatric bipolar disorder include the following:

Young Mania Rating Scale
 (YMRS)—an 11-item scale used
 to assess the symptoms of mania
 in children and adolescents ages
 5 to 17; found to be useful initial
 screening tool

- Young Mania Rating Scale-Parent Version (P-YMRS)—an 11-item scale used for assessment of children and adolescents ages 5 to 17 for possible bipolar disorder; adapted from the clinician version of the YMRS; allows parents to rate the severity of manic symptoms and is useful in measuring the impact of interventions;<sup>17,18</sup> useful screening tool but takes into account only parents/caregivers interpretation of symptoms
- Mood Disorder Questionnaire (MDQ)—a 15-item yes/no tool addresses mood symptoms; developed for adults, but adolescents older than age 12 can answer the MDQ;<sup>19</sup> can be used as preliminary screening tool in adolescents
- Washington University in St.
  Louis Kiddie Schedule for
  Affective Disorders and
  Schizophrenia (WASH-UKSADS)—includes mania items
  specific to the developmental
  stage of prepubertal children;<sup>20</sup>
  implementation too time
  consuming to be utilized in
  clinical practice
- Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Life Time Version (K-SADS-PL) assesses current and lifetime psychiatric history; divides the symptoms surveyed into 82symptom screen interview and five supplements to facilitate differential diagnosis; less time consuming and can be utilized in both clinical and research settings
- Mini-International
   Neuropsychiatric Interview
   (MINI)—a short structured
   diagnostic interview based on
   DSM IV and ICD-10 psychiatric
   disorders; 15-minute
   administration time; equally
   useful in research and clinical
   setting; MINI-Kid version useful
   in assessing psychiatric
   disorders, including bipolar
   disorder in youth; has high
   validation and reliability scores

when compared to Structure Clinical Interview for DSM-III-R (patient version).

Medical workup. No lab test or imaging is diagnostic of bipolar disorder, but a careful medical evaluation and relevant laboratory testing is vital to identify any medical conditions or substance use contributing toward the mood symptoms. Negative medical history and normal physical examination make it unlikely that laboratory testing or imaging would have positive findings. Nevertheless, however, establishing baseline physiological parameters can be helpful before the trial of psychotropics.

Complete blood count (CBC), differential with hematocrit, urinalysis, blood urea nitrogen (BUN), serum electrolytes for sodium, potassium, chloride, calcium, phosphate, and carbon dioxide content; liver function test for aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and bilirubin; and blood glucose, lipid profile, thyroid stimulating hormone (TSH), and lead levels (in children younger than age 7) are the common laboratory tests performed as part of a comprehensive evaluation and premedication work up. Neuroimaging is considered in cases of abnormal findings from neurological examinations.21

Medical conditions that may imitate mood disorders are included in Table 1.

# CLINICAL SYMPTOMS DESCRIPTION

Mania. Symptoms of mania can include elevated, expansive or irritable mood, easy distractibility, decreased need for sleep, racing thoughts, pressure to keep talking, grandiose delusions, excessive involvement in pleasurable but risky activities, poor judgment, and in some cases, hallucinations. Symptoms of depression can include pervasive sadness and crying spells, sleeping too much or inability to sleep, agitation, irritability,

withdrawal from activities formerly enjoyed, drop in grades, inability to concentrate, thoughts of death and suicide, low energy, and significant changed in appetite. 13,22,23 Elated children may laugh hysterically and act infectiously happy without any reason at home, school, or in church. If someone who did not know the child saw the child's behaviors, he or she may think the child was on his or her way to an amusement park. Grandiose behaviors in children include acting as if the rules do not pertain to them. For example, they believe they are so smart that they can tell teachers what to teach, tell other students what to learn, and command the school principal to fire the teachers they do not like. Flight of ideas is when children jump from topic to topic in rapid succession when they talk, and it happens even in absence of a special event. For flight of ideas, ask whether topics of discussion change rapidly, in a manner quite confusing to anyone listening. For an interviewer not so familiar with a child and his or her cultural background, it is imperative to determine whether a parent or other knowledgeable adult can easily follow the stream of words. Racing thoughts are expressed in more concrete terms by children. He or she might say, "It's hard to do anything because my thoughts keep distracting me." A decreased need for sleep is manifested in children who sleep only 3 to 5 hours and are not tired the next day. Whereas children with other forms of insomnia (due to inadequate sleep hygiene, excessive environmental stimuli, anxiety, depression, or ADHD) may lie in bed trying to sleep, children in a manic state are on the computer, talking on the phone, rearranging the furniture in their rooms or in other rooms in the house, or watching television (often with sexual content). Hypersexuality can occur in children with mania without any history of physical or sexual abuse. 22,23 Children act flirtatious beyond their

# TABLE 1. Brief chart of medical conditions imitating mood disorders

### **NEUROLOGICAL**

- Migraine
- Multiple sclerosis
- Brain neoplasm (primary or metastatic)
- Epilepsy (especially temporal lobe)
- Head trauma
- Cerebrovascular disorders

### **ENDOCRINE**

- Hypothyroidism
- Hyperthyroidism
- Pheochromocytoma
- Pregnancy

### **INFECTIONS**

- AIDS
- Infectious mononucleosis
- Brain abscess
- · Systemic bacterial infection, viremia

### METABOLIC AND SYSTEMIC

- Hepatic encephalopathy
- Hepatolenticular degeneration (Wilson's Disease)
- Hypoxemia (chronic pulmonary disease)

# TOXIC

- · Intoxication or withdrawal associated with drug or alcohol abuse
- Adverse effects of prescribed and over-the-counter medications
- Environmental toxins

### **AUTO-IMMUNE**

· Systemic lupus erythematosus

years, may try to touch the private parts of adults (including teachers), and often use explicit sexual language. Hypersexual behavior frequently has an erotic, pleasure-seeking quality to it, whereas the hypersexual behavior of children who have been sexually abused is often anxious and compulsive in nature. <sup>22,23</sup> Manic children can show an increase in goal-directed activities, such as drawing copiously, building extremely elaborate and extensive Lego towns, or writing novels in a short period of time.

With regard to psychomotor agitation, it should represent a distinct change from their baseline. In addition to core symptoms of mania, psychotic symptoms, including hallucinations and delusions, can be present in children with bipolar disorder. <sup>22,23</sup> Though there is lot of variability in reported cases of psychosis in pediatric bipolar disorder, psychosis has been reported in 16 to 60 percent of bipolar youth. Auditory hallucinations have been reported as the most common psychotic

symptom.24 Psychotic features have been found to be less common in adolescents compared to adults and even less common in children compared to adolescents.<sup>24</sup> It is useful to distinguish benign perceptual distortions that are nonimpairing and are not considered signs of psychosis. Although not a core symptom of mania, children with bipolar disorder are at extremely high risk of suicidal ideation, intent, and plans. Most of suicide attempts seem to occur during a depressed or mixed episode or when the child is psychotic.<sup>22,25</sup> Irritable mood is a universal part of childhood psychopathology. But one has to remember that any hot, hungry, stressed, or tired child with or without psychopathology will show irritable mood. A distinct feature of irritability in children with bipolar disorder is extremely aggressive and/or self-injurious behavior. Children with bipolar disorder frequently have extreme rages or meltdowns over trivial matters (e.g., a 1- to 2-hour tantrum after being asked to tie his or her shoes). 13,22,23

Symptoms interpretation. Irritability and emotional lability have been described as the most common symptoms, while elated mood and grandiosity have been described as the most cardinal symptoms in pediatric bipolar disorder. Euphoria, elation, paranoia, and grandiose delusions are much less common in younger children. Similarly vegetative symptoms are comparatively less in prepubertal children compared to postpubertal children. 13,22,23,26,27

**Mood cycling.** Studies suggest that it is common for children with bipolar disorder to have multiple mood episodes during the same day. The mood may fluctuate from giddy, silly highs to feeling gloomy and suicidal. Clear differentiation between episodes of mania and depression may be lacking (e.g., irritability and aggression may be present in both mania and depression). 13,22-24,26,27 Studies describe some of the variants of

cycling as ultra rapid cycling (e.g., 5–364 cycles per year), ultra complex cycling (e.g., presence of short cycles embedded within a more prolonged cycle or episode). or ultra-radiant cycling (e.g., mania that occurs for more ≥4 hours per day).28 Unfortunately, DSM-IV does not recognize such rapidity in cycling. Leibenluft29 suggested defining pediatric bipolar disorder as "narrow," "intermediate," and "broad" phenotypes. Narrow phenotype is attributed to those who meet full criteria based on DSM-IV. Intermediate phenotype includes two subcategories—those with hallmark symptoms of short duration (e.g., 1-3 days) and those with episodic irritable mania or hypomania meeting the duration criteria without elation. Broad phenotype consists of nonepisodic and chronic symptoms of severe irritability and hyperarousal. Bipolar disorder, not otherwise specified (BP-NOS), category in DSM-IV corresponds to the intermediate and broad phenotypes.

## **COMORBIDITY**

Among children with bipolar disorder, Carlson<sup>30</sup> reported 91 percent with comorbid ADHD; Wozniak<sup>26</sup> reported 98 percent with co-morbid ADHD; and West<sup>31</sup> reported 57 percent with comorbid ADHD (in adolescents). Among youth with ADHD, Biederman<sup>32</sup> reported a 23-percent, Butler<sup>33</sup> reported a 22-percent, and Wozniak<sup>26</sup> reported a 20-percent rate of comorbid bipolar disorder. Overlapping features seem to be easy distractibility, high degree of motor activity, impaired attention, poor impulse control, rapid or pressure speech, and high irritability.34-37 Unfortunately it is almost impossible to differentiate "pressure to keep talking" ([hypo] mania) and "often talks excessively" (ADHD), psychomotor agitation ([hypo] mania) and "often runs about or climbs excessively" (ADHD), and distractibility (both [hypo] mania and ADHD).

Ideally, to make the diagnosis of

TABLE 2. Symptoms of ADHD and pediatric bipolar disorder			
SYMPTOM	PEDIATRIC BIPOLAR	ADHD	
Elevated mood	Common with element of grandiosity	Much less common	
Hypersexuality	Common	Not seen	
Psychotic symptoms	Common	Not seen	
Irritable mood	Very prominent	Less prominent	
Self-injurious/suicidal behavior	Common	Rare	
Family history	Bipolar disorder and depression common	ADHD/ADD	
Flight of ideas/racing thoughts	Could be present	Not seen	

pediatric bipolar disorder with confidence, clinicians should be able to rely on periodicity as part of DSM-IV criteria (since ADHD is not an episodic illness). However, based on review of all relevant studies, most of the time pediatric bipolar disorder present with chronicity of symptoms. 22,23 Research suggests that identification of symptoms that occur exclusively in (hypo) mania like grandiosity, elated mood, flight of ideas, decreased need for sleep, hypersexuality, and increased goaldirected activity can be vital in reaching the correct diagnosis (Table 2). 13,22,34-37 Determining family history of bipolar disorder is also very important.

Another common and often ignored comorbid diagnosis in pediatric bipolar disorder is conduct disorder. Carlson<sup>37</sup> reported conduct disorder as a comorbid diagnosis in 74 percent of children with bipolar disorder, while Kovacs<sup>38</sup> reported 69 percent with comorbid conduct disorder. Overlapping symptoms are irritability, hostility, and impulsivity. <sup>37-39</sup> Interestingly, in youth when overlapping symptoms like hypersexuality and impulsivity

are interpreted as inappropriate sexual behavior or disinhibited social interaction, more likely they would be considered as part of conduct disorder rather than pediatric bipolar disorder. The main differentiating feature between conduct disorder and bipolar disorder is the lengthy prodromal period in conduct disorder with progression from less to more severe rule breaking, whereas mania mostly presents as abrupt onset of impulsive behavior.<sup>39</sup>

### DIAGNOSTIC VALIDITY

Longitudinal studies of an illness like pediatric bipolar disorder are key components to affirm the validity of the diagnosis. That is perhaps the only way many questions related to course of illness can be answered. To date, two notable prospective studies have been performed that investigated the course and outcome of pediatric bipolar disorder.

A four-year, prospective, longitudinal study<sup>40</sup> examined 86 subjects (mean age 10.8 years) with bipolar disorder who were all assessed at six, 12, 18, 24, 36, and

TABLE 3. Differences between pediatric and adult bipolar disorder

	PEDIATRIC BIPOLAR DISORDER	ADULT BIPOLAR DISORDER
Onset	Prepubertal, early adolescent	Late adolescence or early 20s
Nature of symptoms	Longer symptomatic stage	Episodic in nature—long asymptomatic stage between episodes not uncommon
Mixed episodes (concurrent depression/ manic symptoms)	Very common	Relatively less common
Psychotic symptoms	Less common	More common
Family history of bipolar disorder	Common	Common though less common than in pediatric bipolar disorder
ADHD comorbidity	60–90%	Relatively less common
Bipolar subtype stability	Unstable—change from Bipolar NOS to Bipolar Type I or II common	Relatively more stable

48 months. The phenotype was defined as DSM-IV bipolar I disorder (manic or mixed) with at least one cardinal symptom (elation and/or grandiosity) to ensure differentiation from ADHD. Prospective episode duration of manic diagnoses, using onset of mania as baseline date, was 79.2±66.7 consecutive weeks. Bipolar diagnosis occurred during 67.1±28.5 percent of total weeks, during the 209.4±3.3 weeks of follow-up. Throughout the study, all subjects continued to meet criteria for bipolar disorder I, with 87.2 percent recovering from initial episode, but 72 percent relapsing during the four years. Findings validate the existence of longepisode duration and chronicity of pediatric mania.

Another study<sup>41</sup> (COBY) was done to assess the longitudinal course of pediatric bipolar subtypes (BP-I, BP-II, and BP-NOS). Two-

hundred and sixty children (mean age 13) were assessed every nine months over two years. Results showed that 70 percent of subjects recover and 50 percent had at least one syndromal recurrence. BP-1 and BP-II had more recurrences, while BP-NOS had more prolonged symptomatic course. Over the follow-up period, 20 percent of those with BP-II converted to BP-I, 18.5 percent of those with BP-NOS converted to BP-I, and 6.5 percent of those with BP-NOS converted to BP-II. Early-onset BP, BP-NOS, long duration of mood symptoms, low socioeconomic status, and psychosis were associated with poorer outcomes and more rapid mood changes.

# **CONCLUSION**

The presentation of bipolar disorder in youth is mostly atypical compared with that of the classic adult disorder (Table 3). Children

who receive a diagnosis of bipolar disorder typically present with rapid fluctuations in mood and behavior, often associated with comorbid ADHD and disruptive behavior disorders. This atypical but common presentation of pediatric bipolar disorder seems to be related to developmental differences in manic symptom expression and the evolving picture of this disorder in children.

One should not forget that the question of diagnostic continuity has important treatment and prognostic implications. Prospective longitudinal studies done over the span of 2 to 4 years seem to affirm that youths diagnosed with bipolar disorder show a continuum of bipolar symptom severity with frequent fluctuations of mood symptoms. Results provide validation of diagnosis of pediatric bipolar disorder.

Our opinion is that an increase in clinician comfort level and familiarity with diagnosis of pediatric bipolar disorder as well as more frequent use of BP-NOS diagnosis<sup>42</sup> in youth who do not have the classic adult presentation are the possible reasons for rapid increase in cases of bipolar disorder in children.

To sum up, we propose the following steps in evaluation of pediatric bipolar disorder:

Step I—Ask families to keep daily logs (before psychiatric/psychological evaluation) for at least a two-week period, and track mood, activity level, energy, sleep, as well frequency, intensity, duration, and triggers of temper tantrums. Check with child's caregivers about functioning at home, at school, and with peers.

**Step II**—Review past medical records, take good medical history, and order appropriate investigations (as needed), which can include EEG, brain scan, toxin screens, and basic blood work.

**Step III**—Comprehensive interview by clinician knowledgeable about mood

disorders in children/adolescents. It is important to interview both child and parents (caregivers). Pay special attention to family history of mental illness. During evaluation pay special attention to cardinal symptom, like elated mood, grandiosity, racing thoughts, decreased need for sleep, psychosis, and hypersexuality. Also look into intensity of irritable mood and level of aggression. Assess safety issues. Use appropriate instruments/scales as needed.

**Step IV**—Discuss diagnostic impression with family, reason for diagnostic impression, and reassure about possible favorable outcome with proper treatment.

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